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Correlated Neuronal Discharges that Increase Coding Efficiency during Perceptual Discrimination

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Summary

During a sensory discrimination task, the responses of multiple sensory neurons must be combined to generate a choice. The optimal combination of responses is determined both by their dependence on the sensory stimulus and by their cofluctuations across trials—that is, the noise correlations. Positively correlated noise is considered deleterious, because it limits the coding accuracy of populations of similarly tuned neurons. However, positively correlated fluctuations between differently tuned neurons actually increase coding accuracy, because they allow the common noise to be subtracted without signal loss. This is demonstrated with data recorded from the secondary somatosensory cortex of monkeys performing a vibrotactile discrimination task. The results indicate that positive correlations are not always harmful and may be exploited by cortical networks to enhance the neural representation of features to be discriminated.

Introduction

Neurons in primary somatosensory cortex (S1) respond during a vibrotactile discrimination task (Mountcastle et al., 1990; Hernández et al., 1997; Romo and Salinas, 2001) such that their mean firing rates increase monotonically with increasing stimulus frequency (Salinas et al., 2000). Through these variations in rate, single S1 neurons encode the frequency of mechanical vibrations with an accuracy that matches the subject's discrimination performance (Hernández et al., 2000). S1 units that respond to stimuli in the frequency range used in this task (5–50 Hz, the "flutter" range) have rapidly adapting properties associated with Meissner's primary mechanoreceptors (Talbot et al., 1968; Mountcastle et al., 1969).

Neurons in secondary somatosensory cortex (S2) also respond during the same task. Although there is some evidence for parallel inputs to S1 and S2 (Zhang et al., 1996, 2001), in primates S2 seems to be largely driven by S1 (Pons et al., 1987, 1992; Burton et al., 1995). In contrast to S1, neurons in S2 have much larger, typically bilateral receptive fields with more complex characteristics (Sinclair and Burton, 1993; Pruett et al., 2001; Romo et al., 2002). Most importantly, some S2 neurons show rate increases similar to those observed in S1, but for other units the firing rate decreases monotonically as a function of stimulus frequency (Salinas et al., 2000; Romo et al., 2002). When the rates are plotted versus stimulus frequency, these two types of neurons have positive and negative slopes, respectively.

In a previous study (Salinas et al., 2000), we found that single S2 neurons of both types carry significantly less information about stimulus frequency than measured in S1. This observation is confirmed here by comparing the neuronal responses with the subject's discrimination capability (see below). Also, similar increasing and decreasing responses are found in areas central to S2, presumably involved in the discrimination process (Romo et al., 1999; Hernández et al., 2002). The generation of responses with negative slopes and the apparent degradation in the quality of the sensory representation are intriguing, because from the point of view of sensory coding capacity, the sign of the slope by itself does not make any difference; a population with only positive slopes is as accurate as a population with positive and negative slopes.

This, however, does not take into account the correlated noise, that is, the random variations in neuronal responses shared by pairs of neurons. Here we show that generating complementary populations with positive and negative response slopes is actually an optimal coding strategy when their fluctuations are positively correlated, because in that case complementary responses can be subtracted in order to eliminate the common-mode noise. We find that positive correlations are prevalent between somatosensory neurons. This, together with the observation that subtraction seems to be an essential component of this task (Hernández et al., 2002; Romo et al., 2002), suggests that separate responses that increase and decrease with a stimulus feature may be generated, at least in part, to optimize perceptual performance. Thus, although positive correlations may limit the coding capability of neural populations (Zohary et al., 1994), this is not always the case.

Results

Single-Unit Responses

Two monkeys (*Macaca mulatta*) were trained in the vibrotactile discrimination task until their psychophysical thresholds were stable (Mountcastle et al., 1990; Hernández et al., 1997). The time course of an individual trial is schematized in Figure 1A. After training, we recorded 167 neurons in S2 while monkeys performed the task (Mountcastle et al., 1990; Hernández et al., 1997). Their mean firing rates during the first and second stimulus periods were significantly different ($p < 0.05$; Wilcoxon rank-sum test; Siegel and Castellan, 1988) from those in a pretrial control period (500 ms) immediately before the stimulator probe moved down (PD; Figure 1A). In 99 of 167 neurons, the firing rate varied monotonically as a function of the first (f_1) or second (f_2) stimulus frequency (see Experimental Procedures). In 56 of these

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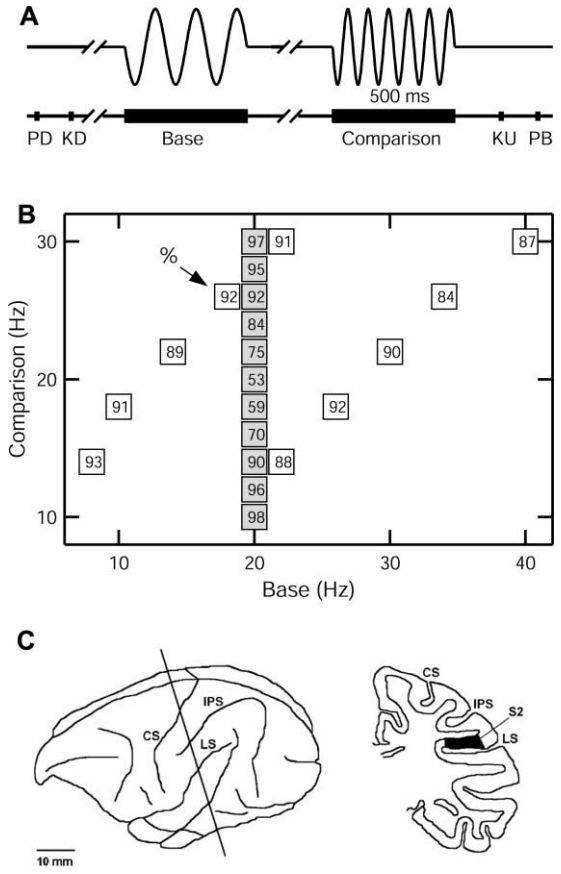

Figure 1. Discrimination Task

(A) Sequence of events during discrimination trials. The mechanical probe is lowered, indenting the fingertip of one digit of the restrained hand (PD); the monkey places its free hand on an immovable key (KD); the probe oscillates vertically at the base stimulus frequency; after a delay, a second mechanical vibration is delivered at the comparison frequency; and the monkey releases the key (KU) and presses either a lateral or a medial push button (PB) to indicate whether the comparison frequency was higher or lower than the base.

(B) Stimulus set used during recordings. Each box indicates a base/comparison frequency pair, with numbers inside the boxes showing overall percent of correct discriminations. Comparison frequencies above and below a fixed base frequency of 20 Hz (gray boxes) were used to construct psychometric curves.

(C) Location of recording sites (black strip at right) in secondary somatosensory cortex (S2); CS, central sulcus; IPS, intraparietal sulcus; LS, lateral sulcus.

neurons (57%), the firing rate increased with increasing f_1 and f_2, while in the other 43 (43%) the rate decreased with increasing f_1 and f_2. Examples of these responses are shown in Figures 2B and 2E. These two subpopulations with positive and negative slopes encoded stimulus frequency through their firing rates.

Comparison between Neuronal and Psychophysical Performance

To measure how accurately these neural signals encoded stimulus frequency, we compared them to the animal's psychophysical performance. First, psychometric curves were generated by plotting the percentage of trials in which the comparison frequency f_2 was called higher than the base f_1, as a function of f_2. For this, only trials in which $f_1 = 20$ Hz were used. Examples of psychometric curves are shown in Figures 2C and 2F. Points near 0% or 100%, where f_1 and f_2 are very different, correspond to easy discriminations, whereas points near 50%, where f_1 and f_2 are very similar, correspond to difficult discriminations. The discrimination threshold is inversely proportional to the maximum steepness of the fitted curve (see Experimental Procedures).

Next, we computed a neurometric function for each neuron using methods from signal detection theory (Green and Swets, 1966; Britten et al., 1992; Hernández et al., 2000; Dayan and Abbott, 2001). For this we considered the responses evoked during stimulus presentation (see Experimental Procedures). The neurometric curve represents the psychophysical performance of an ideal observer that, knowing only the neural responses to f_1 and f_2 in each trial, uses an optimal algorithm to compare them and perform the discrimination task (Green and Swets, 1966; Britten et al., 1992; Hernández et al., 2000; Dayan and Abbott, 2001). In our case, the observer applied the following rule: if the number of spikes evoked during f_2 is higher than during f_1, then the answer should be $f_2 > f_1$; otherwise, $f_2 < f_1$. Using this rule, the observer's responses may be graphed in the same way as the monkey's. Thus, one may compare neuronal and psychophysical performance in the same sets of trials.

Figure 2C shows an example. In this case, the neuron's performance was considerably worse than the animal's, as quantified by the discrimination thresholds: the neurometric threshold was 5.2 Hz and the psychometric one was 2.8 Hz (threshold ratio = 0.53). Overall, the neurons that had positive monotonic responses gave an average neurometric threshold of 4.67 $\pm$ 1.51 Hz (mean $\pm$ SD), whereas the psychometric threshold during the study of these neurons was 3.17 $\pm$ 0.68 Hz (threshold ratio = 0.71 $\pm$ 0.20). Similar values were obtained for the neurons with negative monotonic responses: the average neurometric threshold was 5.07 $\pm$ 1.65 Hz and the psychometric threshold was 3.31 $\pm$ 0.75 Hz (threshold ratio = 0.68 $\pm$ 0.24).

These threshold values (Figure 3) are, on average, nearly twice as large as those obtained from S1 during the same task (threshold ratio = 1.31 $\pm$ 0.94; Wilcoxon, $p < 0.001$; Hernández et al., 2000), even though the criteria for selecting the neurons were the same. This means that the ideal observer performs significantly worse when solving the discrimination task based on the S2 responses than when he listens to the S1 responses. Hence, there is a loss of information from S1 to S2, consistent with previous analyses (Salinas et al., 2000).

Optimal Response Combination

This result is puzzling. First, only 8% of S1 neurons show negative monotonic responses, as opposed to 40% in S2 (Salinas et al., 2000; Romo et al., 2002). It does seem, however, that the S2 responses are driven by those in S1, because (1) in primates, activation of S2 depends strongly on a direct S1 input (Pons et al., 1987, 1992; Burton et al., 1995); (2) during stimulation with periodic mechanical stimuli, S1 neurons typically fire near a spe-

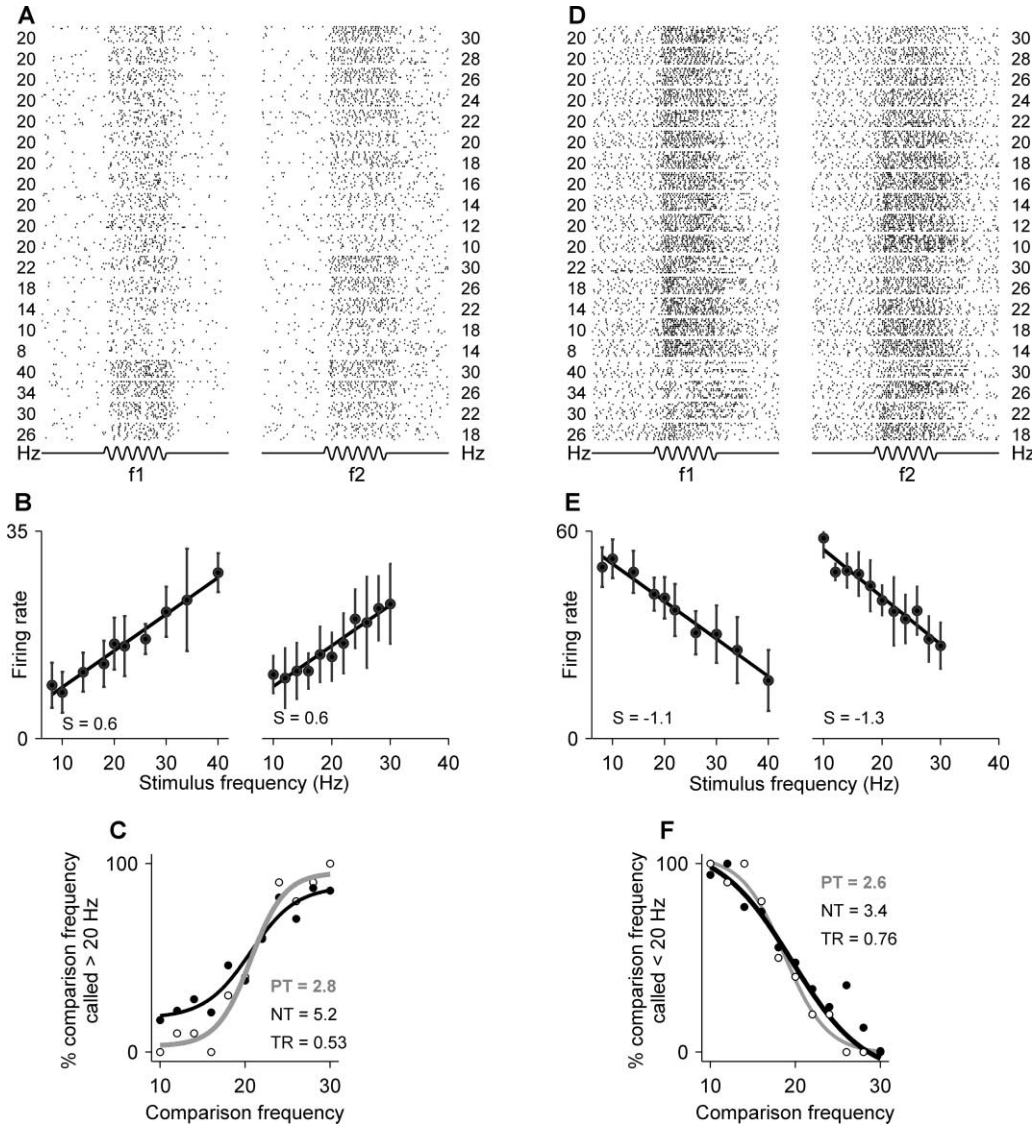

Figure 2. Examples of Neuronal Responses in S2

Responses analyzed were evoked by the first (f_1) and second (f_2) stimulus frequencies during the vibrotactile discrimination task.

(A) Raster plots of an S2 neuron with positive slope. Each row of ticks is a trial, and each tick is an action potential. Trials were delivered in random order. Labels at left and right indicate f_1 and f_2, in Hz.

(B) Mean firing rate (±SD) as a function of f_1 and f_2; S, slope value.

(C) Psychometric and neurometric functions for the responses in (B). Continuous curves are sigmoidal fits (χ^2, $p < 0.001$) to the data points for 11 pairs of stimulus frequencies in which f_1 was fixed at 20 Hz. *y* axis is equivalent to the probability that f_2 is judged higher than f_1. Gray line is psychometric function (subject's performance); black line is neurometric function (ideal observer's performance). PT, psychometric threshold, in Hz; NT, neurometric threshold, in Hz; TR, threshold ratio (PT/NT).

(D–F) Same format as in panels on the left, but for a neuron with negative slope.

cific phase relative to the stimulation cycle (Mountcastle et al., 1969, 1990), much like primary afferents do (Talbot et al., 1968), whereas this phase-locking is virtually absent in S2; and (3) the response latencies of S2 neurons were 48.1 ± 19.6 ms (n = 56, range [30, 110]) for those with positive slopes and 47.8 ± 30.4 ms (n = 43, range [30, 140]) for those with negative slopes, and these latencies were much longer than those of S1 neurons, which averaged 22.9 ± 6.5 ms (n = 69, range [10, 50]). Second, S2 plays a crucial role in somatosensory processing (Ridley and Ettlinger, 1978), and fluctuations in the firing rate of single S2 neurons covary with psychophysical performance on a single-trial basis (Salinas et al., 2000; Romo et al., 2002), which indicates that S2 activity is strongly correlated with behavior during vibrotactile discrimination. Third, dual ensembles of increasing and decreasing responses have also been reported using other somatosensory discrimination tasks (Sinclair and Burton, 1993; Jiang et al., 1997; Pruett et al., 2001). Fourth, areas central to S2 use the same dual representation during the discrimination process (Romo et al., 1999; Hernández et al., 2002). All this suggests that gen-

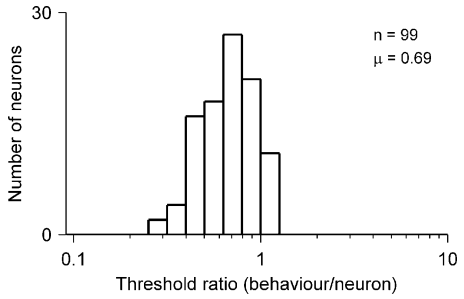

Figure 3. Psychometric/Neurometric Threshold Ratios

Distribution of threshold ratios for n = 99 S2 neurons studied during the discrimination task; μ, mean threshold ratio.

erating both types of responses should have some functional advantage, and it would be surprising if this secondary sensory representation were notoriously less efficient than the primary one.

On the other hand, the apparent loss of information arises when neurons are analyzed one at a time. This loss could be compensated by population mechanisms (Dayan and Abbott, 2001; Parker and Newsome, 1998). Pooling or averaging the responses of a homogeneous neuronal population may improve neurometric thresholds (Tolhurst et al., 1983; Watson, 1990; Britten et al., 1992; Shadlen et al., 1996), but the particular way in which multiple responses are combined is crucial (Abbott and Dayan, 1999). The best way to pool neuronal responses depends on the type and degree of dependency that may exist between them (Parker and Newsome, 1998; Abbott and Dayan, 1999). The two types of monotonic responses found in S2 are ideal to examine this question analytically, because their dependence on the stimulus is simple and because, given the requirements of the task, there is a reasonable hypothesis about the target computation: solving the task is equivalent to calculating the sign of $f_2 - f_1$.

Consider two responses, r_+ and r_-, that are linear functions of stimulus frequency f:

$$r_+ = s_+ f + b_+ + \sigma_+ \gamma_+ \quad (1)$$

$$r_- = s_- f + b_- + \sigma_- \gamma_-. \quad (2)$$

Here, s_+ and s_- are slopes, b_+ and b_- are constant offsets, and γ_+ and γ_- represent Gaussian noise with zero mean and unit variance, so σ_+ and σ_- measure the variability of the corresponding responses. In addition, assume that r_+ and r_- are correlated, as measured by their linear correlation coefficient ρ. Now suppose an observer tries to solve the discrimination task by combining r_+ and r_- linearly in each trial. That is, he computes

$$R = Ar_+ + Br_-, \quad (3)$$

which is a function of frequency, where A and B are constant coefficients. By evaluating this quantity during the two stimulation periods, the observer will determine whether on any given trial $f_2 > f_1$ or $f_2 < f_1$. In this case, the observer's discrimination threshold DT is given by

$$DT = \frac{k\sqrt{\sigma_+^2 + C^2\sigma_-^2 + 2C\sigma_+\sigma_-\rho}}{s_+ + C\,s_-}, \quad (4)$$

(see Experimental Procedures) where $k = 0.95$ and $C = B/A$; this parameter determines the relative weights of r_+ and r_-. Now we may ask what is the mixture of r_+ and r_- that produces optimal performance. To find out, compute the value of C that minimizes DT; the answer is

$$C_{opt} = \frac{\sigma_+^2 s_- - \sigma_+\sigma_- s_+\rho}{\sigma_-^2 s_+ - \sigma_+\sigma_- s_-\rho}. \quad (5)$$

This expression determines the best strategy for the observer.

To compare different strategies, first suppose the variabilities are equal, so $\sigma_+ = \sigma_-$; this does not alter the results qualitatively. Now note that for a single response r_+ ($C = 0$), the threshold is simply $k\sigma_+/s_+$. If the two original responses have identical slopes ($s_- = s_+$), the optimal strategy is to add them ($C_{opt} = 1$), such that

$$DT_{add} = \frac{k\sigma_+\sqrt{1+\rho}}{s_+\sqrt{2}}. \quad (6)$$

But if the slopes have opposite signs ($s_- = -s_+$), the optimal strategy is to subtract ($C_{opt} = -1$), such that

$$DT_{sub} = \frac{k\sigma_+\sqrt{1-\rho}}{s_+\sqrt{2}}. \quad (7)$$

When the two responses are independent ($\rho = 0$), in both cases the threshold decreases by a factor of $\sqrt{2}$, as expected. In this case, a pair of neurons with the same slope (with a given magnitude s) is just as good for discrimination as a pair with slopes of opposite sign (with the same magnitude s)—the former should be added and the latter should be subtracted. However, the result also depends on how the responses covary across trials (Abbott and Dayan, 1999; Zohary et al., 1994), because of the factors $\sqrt{1+\rho}$ and $\sqrt{1-\rho}$. When fluctuations are included, either addition or subtraction is generally better, depending on the sign of ρ. We now compare these calculations with our experimental measurements.

Combining Pairs of Recorded Neurons

In the range of stimulus frequencies used here, S2 responses can indeed be fit using a linear model (Draper and Smith, 1966; Press et al., 1992). On average, for the neurons with positive slopes, $s_+ = 0.85 \pm 0.24$, $b_+ = 9.0 \pm 5.7$, and $\sigma_+ = 5.9 \pm 2.3$ (SD indicates variability in fitted values across the population), whereas for the neurons with negative slopes, $s_- = -1.04 \pm 0.31$, $b_- = 46.3 \pm 11.8$, and $\sigma_- = 6.7 \pm 2.1$, with all rates in spikes/s and frequencies in Hz. The greatest departure from the theoretical model considered above is that the deviations σ_+ and σ_- had a weak dependence on stimulus frequency. However, using multiplicative rather than additive noise in Equations 1–2 leads essentially to the same conclusions (not shown). Crucially, from pairs of S2 neurons recorded simultaneously—from different electrodes—we found the following correlation coefficients: for pairs with positive slopes, $\rho_{++} = 0.12 \pm 0.05$ (n = 8, range [0.05, 0.21]), for pairs with negative slopes, $\rho_{--} = 0.10 \pm 0.04$ (n = 6, range [0.06, 0.17]), and for pairs with positive and negative slopes, $\rho_{+-} = 0.15 \pm 0.1$ (n = 18, range [−0.07, 0.29]). In addition, we also reanalyzed data from a much larger S2 database (Salinas et al., 2000) that included multiple stimulation proto-

Table 1. Additional Correlation Coefficients

Chosen Pairs	ρ_{++}	ρ_{--}	ρ_{+-}
All	0.16 ± 0.3 (410)	0.14 ± 0.3 (370)	0.05 ± 0.21 (720)
With significant correlation	0.5 ± 0.36 (97)	0.47 ± 0.34 (97)	0.23 ± 0.35 (96)
With significant slopes	0.24 ± 0.33 (140)	0.28 ± 0.35 (95)	0.04 ± 0.2 (180)

Data are from neurons used in a previous study (Salinas et al., 2000). Values are mean ± SD, with numbers of pairs for each case in parentheses. Results include multiple stimulus sets and experimental conditions. The significance of individual correlation coefficients and slopes was determined through permutation tests (Siegel and Castellan, 1988). Significance level was set at $p < 0.05$.

cols and several hundred pairs; the results are shown in Table 1. Regardless of the criteria for selecting the pairs, the means of all three correlation types, ρ_{++}, ρ_{--}, and ρ_{+-}, were always positive, which is the key for the analysis presented here. Based on the mean numbers from the 99 linearly tuned neurons, optimal discrimination occurs when $C_{opt} = -0.93$, although practically the same threshold is obtained with a one-to-one subtraction ($C = -1$).

Figure 4 illustrates the effect of subtraction on two neurons recorded simultaneously. One unit had a positive slope: its rate increased with increasing stimulus frequency (Figure 4A). The other unit had a negative slope (Figure 4C). Their firing rates had a linear correlation coefficient of −0.07 (not significant). The corresponding neurometric functions are shown in Figures 4B and 4D. The subtracted data and the corresponding neurometric function are shown in Figures 4E and 4F, respectively; the threshold is lower than for the original individual functions. As expected, subtraction generates a signal that is better suited for discrimination.

When positive correlations are present, the capacity to subtract pairs of neuronal responses is also advantageous for combining units with a wide range of sensitivities; here we mean that C may be negative, although not necessarily equal to −1. For instance, consider an extreme case: one neuron with a positive slope and another with zero slope that is nevertheless correlated with the first one. By itself, the second neuron is useless for discrimination because the average rate does not vary with frequency. However, subtracting the second response from the first one has a beneficial effect: the common noise is eliminated (assuming equal variabilities, $C_{opt} = -\rho$, and DT decreases by a factor of $\sqrt{1 - \rho^2}$).

Thus, subtraction seems to be beneficial as a generalized strategy for combining positively correlated neurons with positive and negative slopes. To investigate

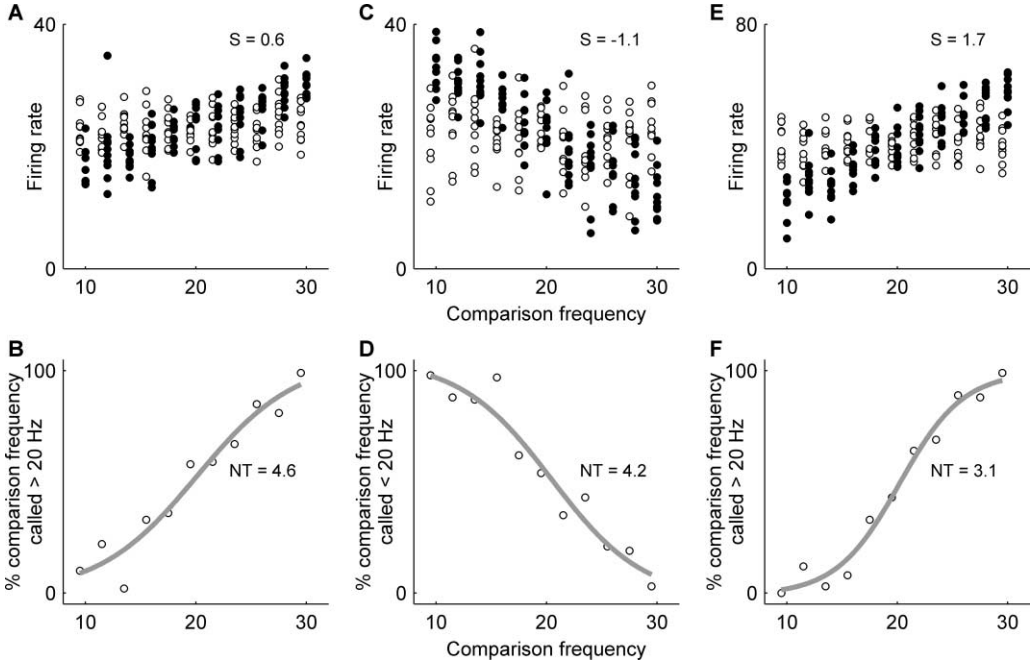

Figure 4. Increase in Discrimination Capacity after Subtraction of Opposite S2 Responses

(A) Firing rates of a neuron with positive slope. Open and filled circles indicate rates evoked during f_1 (fixed at 20 Hz) and f_2, respectively.

(B) Neurometric function for the responses in (A). y axis corresponds to performance of the ideal observer.

(C) Firing rates for a neuron with negative slope.

(D) Neurometric function for the responses in (C).

(E) Responses obtained by subtracting the firing rates in (A) (r_+) minus those in (C) (r_-) plus a constant (differential offset, DO). Open circles correspond to $r_+(f_1) - r_-(f_1) + DO$, whereas filled circles correspond to $r_+(f_2) - r_-(f_2) + DO$.

(F) Neurometric function computed from the subtracted data in (E) (curve is independent of DO). Note the increase in performance and the corresponding lower threshold. NT, neurometric threshold; S, slope.

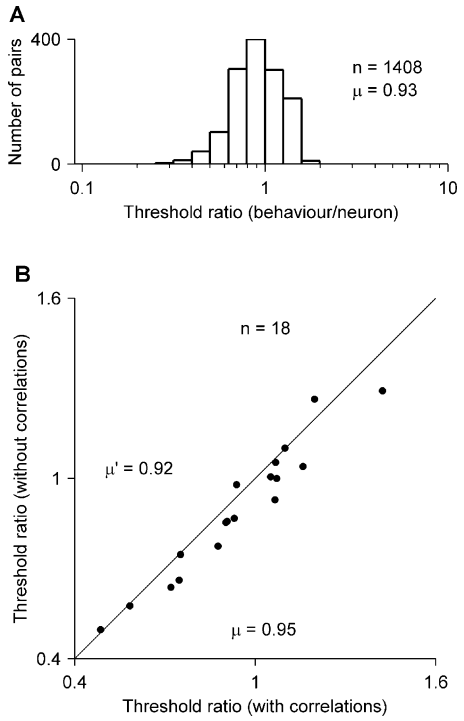

Figure 5. Threshold Ratios for Combined Pairs of S2 Responses

(A) Distribution of threshold ratios for responses generated by subtraction. For each pair of units with positive and negative slopes and recorded separately, a neurometric function was generated from the difference in rates. The threshold ratio was equal to the lower psychometric threshold measured while studying the pair, divided by the neurometric threshold.

(B) The *x* axis shows the threshold ratios generated by subtraction using only the 18 pairs of neurons that were recorded simultaneously and had opposite slopes. The *y* axis shows threshold ratios obtained from the same 18 pairs but with correlations removed, as if they had been recorded in different sessions. The diagonal line indicates equality; μ, mean threshold ratio, μ', mean threshold ratio with correlations removed.

this further, we extended the analysis in Figure 4 to the full population of responsive neurons recorded experimentally. First, we paired neurons with positive and negative monotonic responses excluding the 18 pairs recorded simultaneously, so only independent combinations were generated. For each pair, a direct subtraction ($C = -1$) was performed, a neurometric function was computed, and the resulting neurometric threshold was compared against the lower psychometric threshold obtained for that pair. The resulting distribution of threshold ratios is shown in Figure 5A. The mean ratio was close to 1 and was not significantly different (Wilcoxon, $p > 0.19$) from that obtained from single S1 neurons (Hernández et al., 2000). Thus, two combined S2 signals typically recovered the capacity of a single primary sensory neuron for perceptual discrimination.

We then repeated the procedure using only the 18 pairs of neurons that were recorded simultaneously and had slopes with opposite signs (Figure 5A). In this case, the average threshold ratio was also close to 1. Finally, threshold ratios were calculated for the same 18 pairs but with the correlations removed. This was done by randomly shuffling trials with identical stimulation frequencies. As expected, the resulting mean discrimination threshold became larger (Figure 5B; $p < 0.01$, one-tailed permutation test for paired samples; Siegel and Castellan, 1988). This is a key result, because it confirms that positive correlations may have a favorable effect on discrimination performance.

The Linearity Assumption

A critical question here is how optimal is the linear operation itself; that is, maybe there is a nonlinear function of r_+ and r_- that is much more efficient as a discrimination signal than R in Equation 3. This, however, is not the case. We computed the mutual information, as defined by Shannon (Cover and Thomas, 1991; Dayan and Abbott, 2001; Salinas et al., 2000; see Experimental Procedures), that r_+ and r_- together provide about stimulus frequency, $I(r_+, r_-; f)$, and compared it to the information provided by their difference, $I(R; f)$. These quantities were calculated for multiple pairs of neurons with positive and negative slopes. First, when the subtraction for each pair was optimal ($C = C_{opt}$), the two information measures were identical ($I(r_+, r_-; f) = I(R; f) = 1.11 \pm 0.52$ bits; SD indicates variability across 500 pairs). Second, the calculation was repeated including variations in σ_+ and σ_- as functions of stimulus frequency, like those observed experimentally. This decreased $I(R; f)$ by only ~10% ($I(r_+, r_-; f) = 1.08 \pm 0.30$; $I(R; f) = 0.96 \pm 0.27$ bits). Finally, when σ_+ and σ_- varied with frequency and a direct subtraction was used for all pairs ($C = -1$), the average information provided by the difference was still equal to ~80% of the maximum ($I(R; f) = 0.88 \pm 0.36$ bits). Because mutual information takes into account the full response probability distributions, these results imply that it is impossible to construct a function of r_+ and r_- that, however complicated, would increase discrimination performance by much. With linear tuning, Gaussian noise, and positive correlations, subtraction is optimal, or nearly so, even when compared to other, nonlinear coding strategies.

Discussion

Previously, Zohary et al. (1994) reported positive correlation coefficients in visual neurons on the order of 0.12 and noted that such correlations would seriously limit the beneficial effect of adding or averaging responses with similar tuning (Zohary et al., 1994). Averaging would be optimal—that is, the limitation would vanish—if responses with similar tuning but negatively correlated fluctuations were prevalent (Zohary et al., 1994; Abbott and Dayan, 1999), but this does not seem to be the norm (Gawne and Richmond, 1993; Zohary et al., 1994; Salinas et al., 2000). However, the present observations show that not all positive correlations are deleterious. The S2 circuitry generates two classes of neurons, which have opposite slopes. When paired across classes, these neurons typically have positive correlations, and thus their proper combination produces a signal that is actually better than would be obtained in the absence of these correlations. Here we only considered pairs of neurons, but in general, if there are two populations of oppositely tuned neurons whose responses are subtracted, positive correlations across types offset, at

least in part, the loss in accuracy caused by positive correlations within types (see Experimental Procedures). The subtraction of responses with opposite slopes is beneficial not only because it enhances the signal, which the addition of responses with similar slopes can do as well, but also because it reduces positively correlated noise, which addition cannot do. Thus, it works much like common-noise rejection in differential amplifiers used in electronic circuits. All this suggests that a subtraction must take place downstream from S2.

The activity observed during later stages of the discrimination process is consistent with this idea. This is based on two observations. First, note that we have focused on the subtraction of two different response types, but recall that the ideal observer takes into account both stimulation periods, so his optimal response ends up depending on the sign of $s_+(f_2 - f_1) - s_-(f_2 - f_1)$ + noise (see Experimental Procedures); this is equal to the difference between two quantities that depend on $f_2 - f_1$. Second, other neurons in S2 (Romo et al., 2002) and in premotor (Hernández et al., 2002) and prefrontal (unpublished observations) cortices respond precisely like this, as functions of $f_2 - f_1$: some of these "differential" neurons fire more when $f_2 > f_1$, while others prefer $f_2 < f_1$. The gradual appearance of this differential activity seems to reflect the comparison between the two frequencies (Hernández et al., 2002; Romo et al., 2002). If the monkey's choice is determined by the relative strengths of these differential signals, which seems to be the case, then the monkey would be using the same strategy as the ideal observer: in any given trial, call $f_2 > f_1$ if $s_+(f_2 - f_1) > s_-(f_2 - f_1)$ + noise and call $f_2 < f_1$ otherwise. Thus, the differential responses represent an intermediate step in going from the neurons with positive and negative slopes to the ideal observer's choice. In other words, the monkey's neurons may be performing the same computations as the ideal observer.

The existence of two complementary populations with opposite response distributions has also been discussed by Gold and Shadlen in the context of visual motion discrimination (Newsome et al., 1989; Gold and Shadlen, 2001). In their model, activation of each response type leads to a particular motor action, and the difference between activations represents a decision variable that reflects the sensory evidence in favor of one alternative over the other. In our case, the differential signal enhances the stimulus representation, but the existence of two complementary types of responses at early sensory stages may also be useful for interfacing with more central structures involved in motor processes like those studied by Gold and Shadlen (2001). In prefrontal cortex (Romo et al., 1999), for instance, subtraction can also enhance information about the base stimulus frequency during the working memory period of the discrimination task (unpublished results), and this area communicates with both sensory and motor networks (Miller and Cohen, 2001).

To conclude, we explored the sensory representation in S2, a key somatosensory area central to S1. Initially, this representation, based on two sets of neurons with opposite tuning properties (slopes), seemed disadvantageous; first, because compared to S1, individual S2 cells are less efficient as encoders, and second, because setting aside the fluctuations, there is nothing intrinsically better in a pair of neurons with opposite slopes as compared to a pair of neurons with similar slopes. Both have to be combined properly—by subtraction and addition, respectively—to generate a signal that is useful for discrimination. However, we found that the responses of oppositely tuned neurons are, on average, positively correlated, and this gives a distinct advantage to the subtraction scheme; using this strategy, discrimination performance becomes more accurate. In this condition, correlations become beneficial. Also, there is evidence suggesting that a subtraction is indeed carried out during the task. Exactly how this happens is still an open question that may be key for understanding how sensory and motor processes interact during tactile discrimination.

Experimental Procedures

General

Two monkeys (*Macaca mulatta*) were trained to discriminate the difference in frequency between two mechanical vibrations delivered sequentially to their fingertips; they learned to indicate whether the second frequency was higher or lower than the first (Figure 1A; Hernández et al., 1997; Romo and Salinas, 2001). Neurophysiological recordings were made in S2 contralateral to the stimulation site while monkeys performed the discrimination task. Neurons selected for this study had large cutaneous receptive fields confined to the smooth, hairless skin of the hand. Animals were handled in accordance with the standards of the NIH and the Society for Neuroscience.

Discrimination Task

The paradigm used here has been described before (Hernández et al., 1997; Romo and Salinas, 2001), but briefly, it proceeded as follows. Stimuli were delivered to the skin of the distal segment of one digit of the right, restrained hand, via a computer-controlled Chubbuck stimulator (BME Systems, Inc.; 2 mm round tip). Initial probe indentation was 500 μm. Vibrotactile stimuli were trains of mechanical sinusoids. Stimulus amplitudes were adjusted to equal subjective intensities; for example, 71 μm at 12 Hz and 51 μm at 34 Hz (a decrease of ~1.4% per Hz). In each trial, two vibrotactile stimuli were delivered consecutively, separated by an interstimulus delay of 3 s, and the animal was rewarded for correct discrimination with a drop of liquid. Discrimination results were indicated by pressing one of two push buttons. Performance was quantified through psychometric techniques (Mountcastle et al., 1990; Hernández et al., 1997).

Recording Sessions and Sites

Neuronal recordings were obtained with an array of seven independent, moveable microelectrodes (2–3 MΩ) inserted into S2 (Figure 1C; Mountcastle et al., 1990). Recording sites changed from session to session, and standard histological procedures were used to construct surface maps of all penetrations. This was done, first, by marking the edges of the small chambers (7 mm diameter) placed above the lateral sulcus. Second, in the last recording sessions we made small lesions at different depths in the recorded area.

Data Analysis

Offline analyses and statistical tests were done using custom software written for Matlab (The Mathworks, Natick, MA). Analyses were restricted to the stimulation periods according to the following criteria. For each trial, we calculated the mean firing rates over the stimulation periods. For each stimulus frequency, we computed the mean ± SD of the firing rate over all trials with that frequency. For further analysis, we selected those neurons that had the best linear fits (χ^2, $Q > 0.05$) for firing rate as a function of frequency (Draper and Smith, 1966; Press et al., 1992). We also required that the slopes of the linear fits were significantly different from zero (permutation test [Siegel and Castellan, 1988], $p < 0.05$), and that slopes calculated separately for the two stimulation periods, base and compari-

son, were not significantly different from each other ($p > 0.05$, computed using the SD of the fitted slopes [Draper and Smith, 1966; Press et al., 1992]). Regarding simultaneously recorded neurons, only pairs recorded from different microelectrodes were included in the analysis. The 167 neurons used for this work were from two monkeys; one contributed 61 and the other 106 neurons. Neither animal participated in the study by Salinas et al. (2000). These 167 neurons were studied under identical experimental conditions.

To compute the correlation coefficient of each pair of simultaneously recorded neurons, first we standardized the firing rates of the two neurons by subtracting the mean and dividing by the standard deviation for repetitions of each stimulus frequency. This eliminates correlations due to variations in stimulus strength. Then we calculated the linear (or Pearson's) correlation coefficient (Press et al., 1992) between pairs of standardized values ordered by trial number. Average correlation values computed from responses during the first or second stimulation periods were virtually the same. To verify that these correlations were not due to slow changes in motivation or awareness, we computed a second correlation coefficient for which the standardized scores were further renormalized in blocks of 10 trials (Zohary et al., 1994). This procedure removes correlations arising from slow drift in overall responsiveness but has little effect on the single-trial cofluctuations. Average correlation values calculated using this method were statistically indistinguishable (permutation test $p > 0.08$) from the original ones, which are reported.

Neurometric Curves

We calculated the probability with which, based on the responses of an S2 neuron, an ideal observer would determine correctly whether $f_2 > f_1$. This was done for each combination of f_2 and f_1. The following simple rule, applied in each trial, provides an optimal comparison (Green and Swets, 1966; Dayan and Abbott, 2001): if the number of spikes evoked during f_2 is higher than the number evoked during f_1, then the answer should be $f_2 > f_1$; otherwise, $f_2 < f_1$. Assuming that responses to f_1 and f_2 are independent, each response to f_1 may be paired with all responses to f_2, producing a more robust estimate of the probability of calling $f_2 > f_1$. This probability is equivalent to the area under the ROC curve (receiver operating characteristic), which is the better-known measure of optimal performance (Hernández et al., 2000; Green and Swets, 1966; Dayan and Abbott, 2001). Neurometric data points were generated with this rule; continuous curves were obtained by fitting these points with sigmoidal (Boltzmann) functions (Draper and Smith, 1966; Press et al., 1992). Psychophysical and neuronal discrimination thresholds were defined as half the difference between the stimulus frequency identified as higher than the standard in 75% of the trials and the frequency identified as higher in 25% of the trials (Mountcastle et al., 1990; Hernández et al., 1997). These were read directly, in Hz, from the sigmoidal fits to the neurometric and behavioral data points.

For pairs of S2 neurons recorded simultaneously and with opposite tuning, we calculated the difference in firing rate in each trial and for each frequency. To avoid negative values, a constant offset was added (DO, Figure 4E). This had no effect on the neurometric function, which was calculated from the subtracted rates exactly as done for the single-neuron responses. For pairs of neurons that were not recorded simultaneously, trials corresponding to the same stimulus frequency were paired randomly, and the calculation proceeded as if they had been recorded simultaneously.

For mutual information calculations (Salinas et al., 2000; Dayan and Abbott, 2001; Cover and Thomas, 1991), responses r_+ and r_- were considered equal to the linear functions fitted to the experimental data (Equations 1 and 2) and were randomly paired, with correlation coefficients chosen randomly between 0 and 0.5. Numerical implementation was thus straightforward because all response distributions followed Gaussian statistics.

Theoretical Model

The response R defined by Equation 4 and used by the ideal observer obeys Gaussian statistics, because it is a linear combination of Gaussian variables. Given this, the probability of correct discrimination for the observer (Green and Swets, 1966; Dayan and Abbott, 2001) is equal to $(1/2)\mathrm{erfc}(-d'/2)$, where erfc is the complementary error function and the discriminability d' is given by (Green and Swets, 1966; Dayan and Abbott, 2001)

$$d' = \frac{\langle R(f_2)\rangle - \langle R(f_1)\rangle}{\sigma_R}. \quad (8)$$

Here, the angle brackets indicate an average over trials and σ_R is the standard deviation of R. From Equations 1–3 this is

$$d' = \frac{(s_+ + Cs_-)(f_2 - f_1)}{\sqrt{\sigma_+^2 + C^2\sigma_-^2 + 2C\sigma_+\sigma_-\rho}}. \quad (9)$$

Equation 4 follows from these facts and the definition of the discrimination threshold, with $k = \mathrm{erfc}^{-1}(0.5) - \mathrm{erfc}^{-1}(1.5)$, where erfc^{-1} is the inverse of the complementary error function.

The actual response of the ideal observer depends on the difference $R(f_2) - R(f_1)$. When $C = -1$, this quantity is $(s_+ - s_-)(f_2 - f_1) + \epsilon$, where ϵ is the total Gaussian noise, and can be decomposed as the difference between $s_+(f_2 - f_1) + b + \epsilon_1$ and $s_-(f_2 - f_1) + b + \epsilon_2$, where b is an arbitrary constant. When s_+ is positive and s_- is negative, these two quantities correspond to the firing rates of "differential" neurons preferring the conditions $f_2 > f_1$ and $f_2 < f_1$, respectively. Thus, for $C = -1$, the response of the ideal observer is equivalent to the subtraction or comparison between these two differential signals.

The response R above is based on two neurons, one of each type (+ or −). With more neurons of each type, the correlations between same-type units need to be taken into account. Consider two groups of N neurons each, with units of the same type having identical slopes and variances. In that case,

$$d' = \frac{\sqrt{N}(s_+ + Cs_-)(f_2 - f_1)}{\sqrt{\sigma_+^2(1 + (N-1)\rho_{++}) + C^2\sigma_-^2(1 + (N-1)\rho_{--}) + 2\sigma_+\sigma_- CN\rho_{+-}}}. \quad (10)$$

Note that when $C = -1$, the term with ρ_{+-} counteracts the effect of the other two correlations, which always decrease the discriminability.

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